UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

August 15, 2013

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No. 1677-EUR
DP Barcode: D412105

From: Chris Jiang, Chemist
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Product Science Branch
Antimicrobials Division (7510P)

Chris Jiang
8/15/13

Through: for Karen Hicks, Team Leader
Chemistry and Toxicology Team
Product Science Branch
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To: Demson Fuller PM 32/Nathan Mottl
Regulatory Management Branch II
Antimicrobials Division (7510P)

Applicant: Ecolab Inc.

FORMULATION FROM LABEL:

PC Code	Active Ingredient(s):	% by wt.
014703	Sodium hypochlorite	0.0866
	Inert Ingredients	99.9134
	Total:	100.00

Available chlorine: 0.0825 Free Available Chlorine

CJIANG 8/15/13

BACKGROUND: Ecolab, Inc, has submitted an acute toxicity package to register this non-integrated end-use product. The package includes a cover letter, a label, a Confidential Statement of Formula, an acute oral toxicity study (MRID 49089532), an acute dermal toxicity study (MRID 49089531, an acute inhalation study (MRID 49089529), a primary eye irritation study (MRID 49089533), a primary dermal irritation study MRID 49089534), and a dermal sensitization study (MRID 49089530). The product is a dilution of 1677-52.

RECOMMENDATIONS:

1. The acute toxicity profile for 1677-EUR is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	49089532	III	Acceptable
Acute Dermal Toxicity	49089531	III	Acceptable
Acute Inhalation Toxicity	49089529	IV	Acceptable
Primary Eye Irritation	49089533	IV	Acceptable
Primary Skin Irritation	49089534	IV	Acceptable
Dermal Sensitization	49089530	Nonsensitizer	Acceptable

LABELING

1. The signal word is **CAUTION**.

2. The precautionary labeling must read, " Harmful if swallowed or absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove and wash contaminated clothing before reuse."

3. The first aid statements must read:
   If on skin:
   -Take off contaminated clothing.
   -Rinse skin immediately with plenty of water for 15-20 minutes.
   -Call a poison control center or doctor for treatment advice.
   If swallowed:
   -Call a poison control center or doctor immediately for treatment advice.
   -Have a person sip a glass of water if able to swallow.
   -Do not induce vomiting unless told to by a poison control center or doctor
   -Do not give anything by mouth to an unconscious person.

4. The following first aid statements are optional:
   If inhaled:
   -Move person to fresh air.
   -If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.
   -Call a poison control center or doctor for further treatment advice.

If in eyes:

-Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.

-Call a poison control center or doctor for treatment advice.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (81-1, 870.1100)

Product Manager: Demson Fuller
MRID No.: 49089532

Reviewer: Chris Jiang
Date: January 18, 2013
Study No.: 0406RES31.002

Testing Laboratory: Calvert Laboratories, Inc.
Author: Rene E. Vasquez

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: XY-12, batch number J041021, yellow liquid
Dosage: 550 mg/kg, 2000 mg/kg

Species: Female Sprague-Dawley rats
Age: Eight to nine weeks
Weight: 183 to 185 grams at study start
Source: Harlan

Conclusions:

1. **LD_{50} (mg/kg):** $LD_{50} > 2000$ mg/kg
2. **The estimated LD_{50} is greater than 2000 mg/kg mg/kg.**
3. **Toxicity Category**: III **Classification**: Acceptable

Procedure (Deviations from 81-1): The Up-and-Down Procedure was used. Females were used because they are more sensitive than males. Temperature and relative humidity was outside of the protocol range. These deviations had no impact on the integrity of the study.

Results:

Reported Mortality

Animal Number	Dosage (mg/kg)	Short-Term Outcome	Long-Term Outcome
1872F	550	O	O
1873F	2000	O	O
1874F	2000	O	O
1875F	2000	O	O

O = lived, **X** = died

Observations:

550 mg/kg: The animal appeared normal throughout the study.

2000 mg/kg: These animals appeared normal throughout the study.

Gross Necropsy Findings:

All gross necropsies were unremarkable.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (81-2, 870.1200)

Product Manager: Demson Fuller
MRID No.: 49089531

Reviewer: Chris Jiang
Date: January 22, 2013
Study No.: 0422RES31.002

Testing Laboratory: Calvert Laboratories, Inc.
Author: Rene E. Vasquez

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: XY-12, batch number J041021, yellow liquid
Dosage: 2000 mg/kg

Species: Five male and five female Sprague-Dawley rats
Age: Seven to eight weeks
Weight: ♂: 216 to 229 grams at study start; ♀: 206 to 232 at study start
Source: Harlan

Conclusions:

1. **LD_{50} (mg/kg):** **Males** > 2000 mg/kg
   Females > 2000 mg/kg
   Combined > 2000 mg/kg
2. **The estimated LD_{50} is greater than 2000 mg/kg.**
3. **Toxicity Category**: III **Classification**: Acceptable

Procedure (Deviations from 81-2): Temperature and relative humidity was outside of the protocol range. Mortality checks were inadvertently not performed. The ages of the rats were younger than the ages specified in the guidelines, but were within the body weight range stated in the protocol. These deviations had no impact on the integrity of the study.

Results:

Reported Mortality

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: No dermal irritation was observed. All animals appeared normal throughout the study.

Gross Necropsy Findings: Gross necropsies were unremarkable.

DATA REVIEW FOR ACUTE INHALATION TOXICITY (§81-3, 870.1300)

Product Manager: Demson Fuller
MRID No.: 49089529

Reviewer: Chris Jiang
Study Completion Date: March 6, 2013
Study No.: WIL-862006

Testing Laboratory: WIL Research
Author: Andrew J. Smith

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: XY-12, lot number J071021-2, translucent pale yellow liquid
Nominal Concentration: 3.5 mg/L **Gravimetric Concentration**: 2.1 mg/L

Species: Five male and five female CrI:CD(SD) albino rats
Age: Ten weeks
Weight: ♂: 359 to 387 grams at study start; ♀: 210 to 229 grams at study start
Source: Charle River Laboratories, Raleigh, NC

Summary:

1. **LC_{50} (mg/L)** : > 2.1 mg/L
2. **The LC_{50} is greater than 2.1 mg/L.**
3. **MMAD**: 1.3 ± 1.99 µm
4. **Toxicity Category**: IV **Classification**: Acceptable

Procedure (Deviations from 81-3): A different lot was used than in the other acute toxicity studies. Relative humidity was outside the range specified in the protocol. These deviations had no impact on the integrity of the study.

Results:

Reported Mortality

Dosage (mg/L)	(Number Deaths/Number Tested)		
	Males	Females	Combined
2.1	0/5	0/5	0/10

Chamber Atmosphere			
Dose Level (mg/L)	MMAD (µm)	GSD (µm)	particles < 3.30 µm
2.1	1.4	1.99	87.2
2.1	1.1	1.99	92.4

Chamber Environment During Exposure

Chamber Volume (L)	7.9
Average Total Airflow Volume (Lpm)	45.1
Oxygen Content	20.9
Mean Temperature (°C)	21
Mean Relative Humidity (%)	73

Clinical Observations:

Clinical observations were unremarkable during exposure for all animals. Post-exposure, the males were observed with a wet clear material on the dorsal rump, on the hindlimbs, in the urogenital area and a dried red material around the facial area. Post –exposure, One female was observed with a dried red material around the eyes.

Gross Necropsy Findings:

Gross necropsies were unremarkable with the exception of one female that had clear fluid contents in the uterus.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (81-4, 870.2400)

Product Manager: Demson Fuller
MRID No.: 49089533

Reviewer: Chris Jiang
Date: March 20, 2012
Study No.: 0421LE31.001

Testing Laboratory: Calvert Laboratories, Inc.
Author: Rene E. Vasquez

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: XY-12, batch number J092611-1, yellow liquid
Dosage: 0.1 mL

Species: Three male New Zealand White rabbits
Age: Eleven weeks at time of dosing
Weight: 2.3 to 2.5 kg at study start
Source: Millbrook

Summary:

1. **Toxicity Category**: IV
2. **Classification**: Acceptable

Procedure (Deviations from 81-4): Clinical observations and mortality/morbidity observations were recorded beyond the 72-hour timepoint. The ages of the rabbits were younger than the ages specified in the guidelines, but were within the body weight range stated in the protocol. These deviations had no impact on the integrity of the study.

Results:

Individual Scores for Ocular Irritation

Observations	Rabbit No. 395 (Male)				Rabbit No. 396 (Male)				Rabbit No. 397 (Male)			
	Hours After Treatment											
	1	24	48	72	1	24	48	72	1	24	48	72
I. Corneal Opacity	0	0	0	0	0	0	0	0	0	0	0	0
II. Iritis	0	0	0	0	0	0	0	0	0	0	0	0
III. Conjunctivae												
A. Redness	1	1	0	0	1	0	0	0	1	0	0	0
B. Chemosis	1	0	0	0	1	0	0	0	1	0	0	0
C. Discharge	1	1	0	0	2	0	0	0	0	0	0	0

DATA REVIEW FOR PRIMARY SKIN IRRITATION TESTING (81-5, 870.2500)

Product Manager: Demson Fuller
MRID No.: 49089534

Reviewer: Chris Jiang
Date: March 20, 2012
Study No.: 0420LE31.001

Testing Laboratory: Calvert Laboratories, Inc.
Author: Rene E. Vasquez

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: XY-12, batch number J092611-1, yellow liquid
Dosage: 0.5 mL

Species: Three male New Zealand White rabbits
Age: Ten weeks at time of dosing
Weight: 2.2 to 2.3 kg at study start
Source: Millbrook

Summary:

1. **Toxicity Category**: IV
2. **Classification**: Acceptable

Procedure (Deviations from 81-5): Mortality/morbidity observations was inadvertently missed. The ages of the rabbits were younger than the ages specified in the guidelines, but were within the body weight range stated in the protocol. These deviations had no impact on the integrity of the study.

Results:

Animal number	Erythema/edema after unwrap			
	30-60 min	24 hr	48 hr	72 hr
391/M	0/0	0/0	0/0	0/0
390/M	0/0	0/0	0/0	0/0
389/M	0/0	0/0	0/0	0/0

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (81-6, 870.2600)

Product Manager: Demson Fuller
MRID No.: 49089530

Reviewer: Chris Jiang
Date: January 22, 2013
Study No.: 00424GE31

Testing Laboratory: Calvert Laboratories, Inc.
Author: Rene E. Vasquez

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: XY-12, batch number J071021, yellow liquid
Positive Control: 1-chloro-2,4-dinitrobenzene (DNCB)

Species: Hartley guinea pig
Weight: ♂: 508 g to 615 g; ♀: 440 g 522 g
Age: Eight weeks on Day 1
Source: Elm Hill Breeding Laboratories, Chelmsford, MA

Method: Buehler Method

Summary:

1. **This Product is not a dermal sensitizer.**
2. **Classification**: Acceptable

Procedure (Deviation From §81-6): The initial weight of the animals was above the weight range in the protocol, but the age range was within the protocol range. Relative humidity and temperature were outside of the protocol range at times. A depilatory was used for hair removal. A different lot was used than in the other acute toxicity studies. The Sponsor was contacted and the company was okay with the switching of the batches. These deviations had no impact on the integrity of this study.

Procedure: After preliminary tests, the definitive study was undertaken. Once each week for three weeks, either the 0.3 mL of the undiluted test material or nothing was applied to the clipped left front shoulder using Hilltop chambers and occlusive patches. After chamber application, the trunks of the animals were wrapped with elastic wrap that was secured with adhesive tape. After the exposure period, the chambers and bindings were removed and the test sites were cleansed of residual test substance. The guinea pigs were scored at 24 and at 48 hours after each induction.
Twelve days after the last induction, all animals were challenged with 0.3 mL of the undiluted test substance on the right hind flank. The guinea pigs were scored at 24 and at 48 hours after challenge.

Results: At 24 hours and at 48 hours after each induction, there was no irritation. At 24 hours and at 48 hours after challenge, there was no sensitization response.

The concurrent positive control showed appropriate results using 0.3 mL DNCB in 80 % ethanol during the induction phase and using 0.2 mL of DNCB in acetone during the challenge phase.